

## HEPATITIS A AND HEPATITIS E

### ✓ DISEASE AND EPIDEMIOLOGY

#### **Clinical Description:**

##### **Hepatitis A Infection:**

Hepatitis A is a self-limiting illness characterized by sudden onset of symptoms including malaise, fever, nausea, and diarrhea. Jaundice, characterized by yellowing of the skin or whites of the eye, dark urine, and clay-colored stool, may follow a few days after initial symptoms. Hepatitis A causes disease with varying severity. Generally, symptom severity increases with age. Asymptomatic infections can occur, and are most common in young children. In fact, only 30% of infected children less than 6 years of age will have symptoms of disease. Symptoms typically last for several weeks, however, can last several months in cases with particularly severe disease. Prolonged, relapsing hepatitis for up to one year can occur in some cases, although it is uncommon. Chronic infections are not known to occur. The elderly and persons with chronic liver disease (including chronic hepatitis B or C) are at greater risk of severe hepatitis A and death.

##### **Hepatitis E Infection:**

Infection ranges from subclinical infection to acute illness, including jaundice, anorexia, fever, abdominal pain, and arthralgia (joint pain). The clinical presentation is similar to that of hepatitis A virus (HAV) infection. HEV infection is usually self-limited, and as with HAV infection, chronic infection does not occur. Pregnant women in the third trimester are particularly vulnerable to fatal complications of HEV infection, and the case-fatality rate can reach 20% in this population.

#### **Causative Agent:**

Hepatitis A infection is caused by the Hepatitis A virus (HAV), an RNA virus of the picornavirus family. Hepatitis E infection is caused by the Hepatitis E virus (HEV), a non-enveloped single-stranded positive sense RNA virus. It is related to Norwalk virus and Hepatitis A virus.

#### **Differential Diagnosis:**

Hepatitis has a variety of causes including, but not limited to: viral hepatitises (A, B, C, D, E, X), Epstein-Barr virus, cytomegalovirus, drug-induced hepatitis, toxin-induced hepatitis, auto-immune hepatitis, alcohol liver disease.

## Laboratory identification:

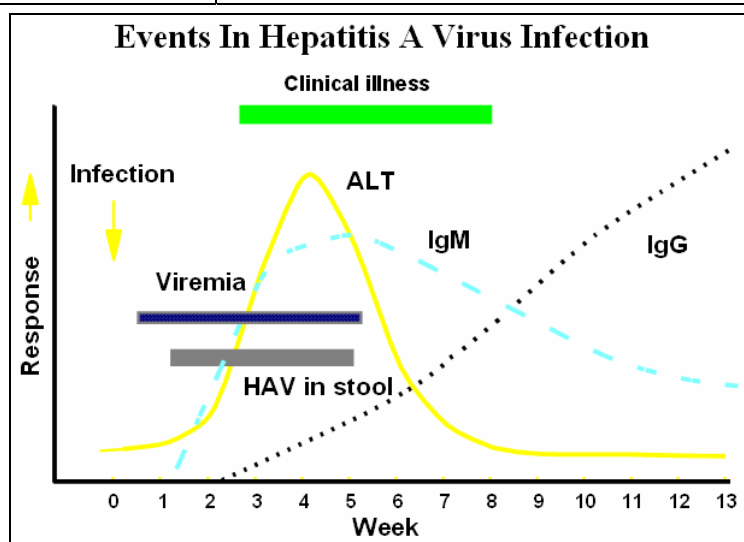
### Hepatitis A:

Hepatitis A cannot be definitively diagnosed without a blood test that measures various serologic markers for hepatitis A virus.

### Serology Panels:

The following table displays the serologic tests available and what their results mean.

Serologic Test	Result
Anti-HAV IgM	<ul style="list-style-type: none"> <li>Diagnostic for acute hepatitis A infection.</li> <li>False positive tests are rare. Anti-HAV IgM is detectable in virtually every case at their first clinical examination.</li> <li>Remains positive for 3-6 months, but can be positive for up to a year.</li> <li>Occasionally positive in adults up to two weeks after receiving hepatitis A vaccine.</li> </ul>
Anti-HAV IgG	<ul style="list-style-type: none"> <li>Not diagnostic for acute hepatitis A infection.</li> <li>Indicates past infection and immunity.</li> <li>Useful to determine immune status of the patient.</li> <li>Positive test results not routinely investigated.</li> </ul>
Anti-HAV Total	<ul style="list-style-type: none"> <li>Not diagnostic for acute hepatitis A infection.</li> <li>Useful to determine immune status of the patient.</li> <li>Positive test results not routinely investigated.</li> <li>Does not differentiate between IgM and IgG antibodies.</li> </ul>
HAV viral antigen tests	<ul style="list-style-type: none"> <li>Detects the presence of antigen in stool.</li> <li>Viral shedding typically completed before the patient seeks medical attention.</li> <li>Test has little routine value.</li> </ul>
Nucleic acid tests (NAT)	<ul style="list-style-type: none"> <li>Not recommended for diagnostic use.</li> </ul>
PCR	<ul style="list-style-type: none"> <li>Not recommended for diagnostic use.</li> </ul>

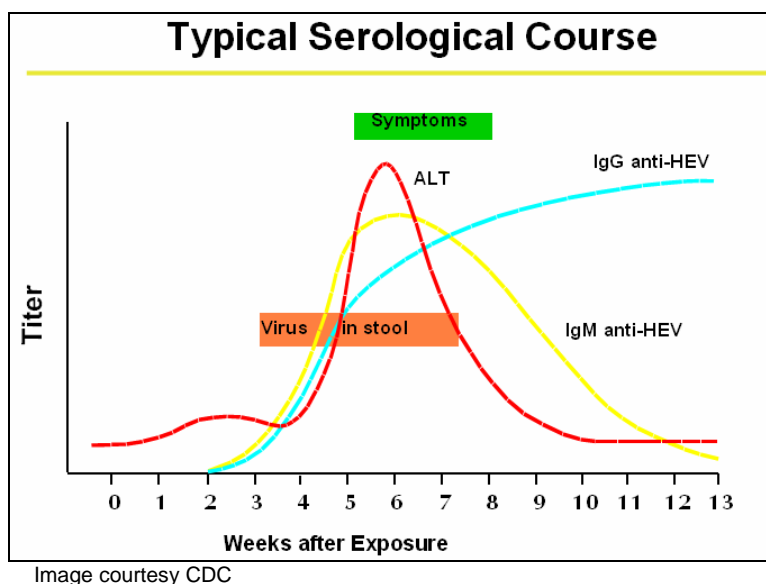


**Chemistry Panels:**

Liver function tests, such as ALT and AST (aminotransferases) are sensitive for liver damage, but are not specific for Hepatitis A. In patients without jaundice, elevated serum aminotransferase levels are required to meet the clinical case definition. The normal value for ALT and AST is up to 50 mIU/mL, but reference ranges can be laboratory specific, so it is appropriate to ask the laboratory performing this test to provide their reference range.

**Hepatitis E:**

No serologic tests to diagnose HEV infection are commercially available in the United States. However, several diagnostic tests are available in research laboratories, including enzyme immunoassays and Western blot assays to detect IgM and IgG anti-HEV in serum, polymerase chain reaction tests to detect HEV RNA in serum and stool, and immunofluorescent antibody blocking assays to detect antibody to HEV antigen in serum and liver.

**Treatment:**

Treatment for hepatitis A and E is supportive.

**Case fatality:****Hepatitis A:**

Generally, hepatitis A is considered a disease with relatively low case fatality. Mortality ranges from 0.1% to 0.3%. For adults over 50, mortality is elevated to 1.8%.

**Hepatitis E:**

Hepatitis E is more severe among pregnant women, especially those in their third trimester. The case fatality rate in this population can reach 20%.

## **Reservoir:**

Humans (and rarely non-human primates) are the only natural host for HAV. In endemic areas, HEV infection has been documented in pigs, cattle, and chickens.

## **Transmission:**

### **Hepatitis A:**

Primary transmission of hepatitis A is by person-to-person spread via the fecal-oral route or through contaminated food or water, which can cause common-source outbreaks.

Cooked foods can also be responsible for transmitting HAV if the food was inadequately cooked or if the food was contaminated after cooking.

- *Intrinsic infection* is when food is contaminated at the point of production or distribution. These outbreaks are usually linked to produce or other foods that are not cooked.
- *Extrinsic infection* of foods occurs at the point of preparation or serving. The foods themselves are not contaminated, but they are contaminated through feces. There is no restriction on which foods could be extrinsically infected. Even cooked foods, if contaminated after cooking, can be the vehicle for an outbreak.

Hepatitis A can also be spread by sexual contact (e.g., oral-anal contact), and among people using illicit drugs – including injection drugs – through close contact, and occasionally, through a blood-to-blood exposure. Bloodborne transmission, although rare, can occur during the viremic phase of the disease. Transfusion-related hepatitis A is quite rare. Intrauterine transmission of HAV has been described.

### **Hepatitis E:**

HEV is transmitted primarily by the fecal-oral route. The most common vehicle documented during outbreaks is contaminated drinking water. While person-to-person transmission is possible, also through the fecal-oral route, it is believed to occur less commonly with HEV than with HAV. The potential for HEV transmission from contaminated food is still under investigation, and there is no evidence of transmission by percutaneous or sexual exposure. Recent evidence also suggests that HEV infection may be transmitted from infected animals through fecal contamination.

## **Susceptibility:**

### **Hepatitis A:**

Infection is thought to provide lifelong immunity. Immunity after vaccination is thought to last at least 10 years in persons who have received the primary vaccine and the booster, but the exact duration of protection has not yet been determined.

### **Hepatitis E:**

Infection is thought to provide lifelong immunity. Travelers to developing countries, particularly in South Asia and North Africa are at higher risk than travelers to other countries. Rare cases have occurred in the United States among persons with no history of travel to endemic countries.

## **Incubation period:**

### **Hepatitis A:**

The incubation period for HAV is 25-30 days, with a range of 15-50 days.

### **Hepatitis E:**

The incubation period for HEV is 26-42 days, with a range of 15-64 days.

## **Period of communicability:**

### **Hepatitis A:**

A person with hepatitis A is generally infectious from 21 days prior to illness onset through 8 days after the onset of jaundice. HAV is shed in stool in greatest amounts during the one to two weeks before the onset of jaundice. Young children often shed HAV asymptomatically, and viral shedding in children may persist for up to 3 months after onset of clinical illness.

### **Hepatitis E:**

The period of communicability for HEV is unknown. However, HEV has been detected in stool 14 days after the onset of jaundice and 4 weeks after the ingestion of contaminated food and water.

## **Epidemiology:**

### **Hepatitis A:**

Hepatitis A infections occur worldwide. Hepatitis A is one of the most commonly identified vaccine-preventable diseases. Rates are highest among children 5 to 14 years of age and lowest among adults older than 40. Actual rates of HAV are unknown, but this disease is presumed to be significantly underreported or under-diagnosed. It is estimated that about a third of the U.S. population is immune to Hepatitis A, through infection or vaccination.

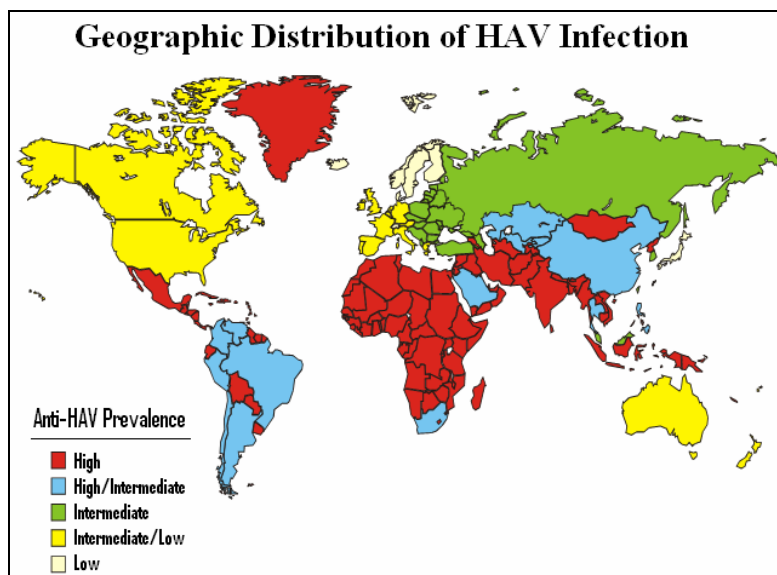


Image courtesy CDC

In developing countries, the disease is usually endemic. Because of this most adults are immune due to prior infection and outbreaks are rare. Hepatitis A outbreaks in developed countries have been linked to food and water sources contaminated with HAV. These foods include tomatoes, green onions, and lettuce. Many outbreaks related to produce have been linked to infected field workers who were not provided adequate toilet facilities. Food may be contaminated at the source of production or the source of preparation. Public and private health systems should be especially vigilant for hepatitis A cases during natural disaster situations in which sewer systems are compromised.

Persons with a high risk for infection include:

- Travelers to regions where hepatitis A is endemic,
- Persons with chronic liver disease
- Men who have sex with men
- Persons using illicit drugs
- Persons with clotting factor disorders
- Daycare workers
- Health care providers for incontinent persons

During the late 1980s and 1990s, hepatitis A rates in Utah were significantly higher than national rates. Since 1998, however, Utah rates have been comparable to U.S. rates.

**Hepatitis A infections per 100,000 persons, Utah and U.S., 1990-2006.**

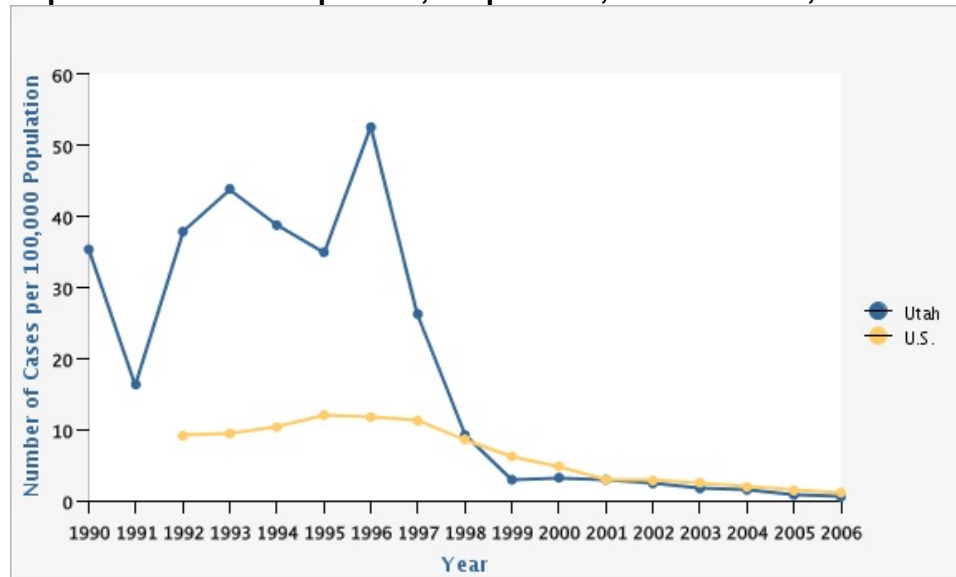


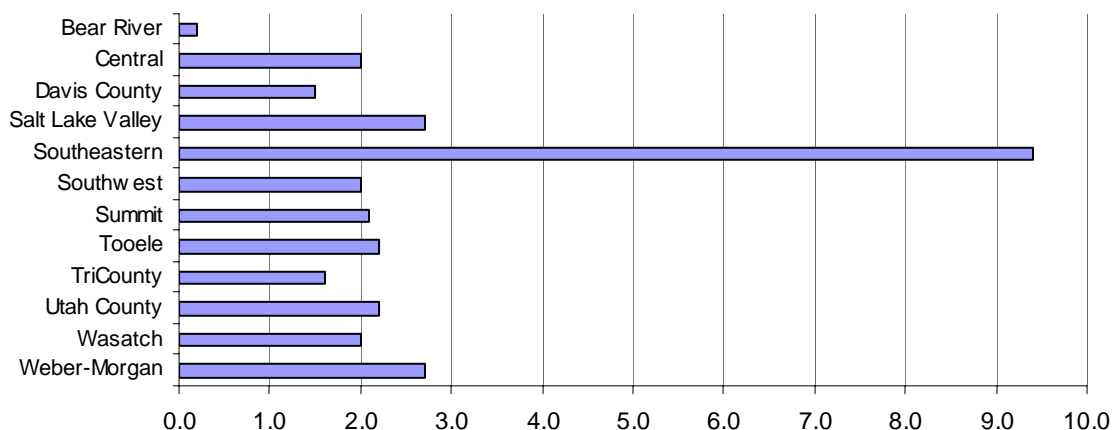
Image courtesy IBIS-PH

This decreasing trend is attributed to improved hygiene during food preparation and greater immunity in the population due to increased use of the hepatitis A vaccine. The trend may also be a result of the natural cycle of the disease.

From 2001 to 2003, the Southeastern Utah Health District reported more hepatitis A infections per 100,000 persons than any other district (9.4/100,000). However, considering the relatively small population, a few cases of infection can affect the rate significantly. Routine public health investigations have not identified a risk factor that puts Southeastern Utah residents at higher risk for hepatitis A infection. Salt Lake Valley and Weber-Morgan health departments each reported 2.7 infections per 100,000 persons.

Bear River Health Department had the lowest rate of infection (0.2/100,000). See the following table for other local health district data.

**Hepatitis A infections per 100,000 persons by Local Health District, State of Utah, 2001-2003.**



**Hepatitis E:**

HEV infection is rare in the U.S. Most reported cases are imported from HEV-endemic countries, where contamination of water is common. However, several cases of acute HEV infection have been reported in individuals with no recent travel outside of the U.S. HEV infection should be considered in any patient with non-A, non-B, non-C hepatitis.

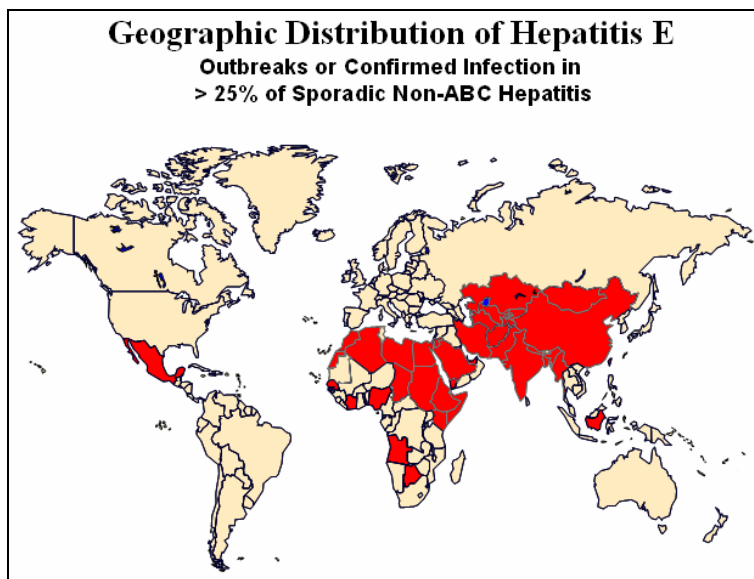


Image courtesy CDC

## ✓ **PUBLIC HEALTH CONTROL MEASURES**

### **Public health responsibility:**

- Identify patient contacts and administer prophylaxis
- Identify the source of infection for the patient and possible other contacts associated with the infection source.

### **Prevention:**

Vaccination is highly effective in preventing hepatitis A. Since HEV cannot be transmitted in the absence of HAV infection, the prevention of HAV infection through immunization is the best way to prevent HEV infection. The best way to prevent infection is through vaccination. However, the vaccine is not 100% effective, and additional measures should also be used to prevent infection and transmission. Persons with acute HAV and/or HEV infections should prevent fecal-oral transmission of the disease by not cooking or serving food for others for up to 8 days after the onset of jaundice. Infected persons should also abstain from sex for up to 8 days after the onset of jaundice to prevent bloodborne transmission.

### **Personal Preventive Measures/Education**

Persons can avoid exposure to the virus by:

- Always washing their hands thoroughly with soap and water before eating or preparing food, after using the toilet, and after changing diapers.
- Washing their own hands as well as their child's hands after changing diapers, and dispose of diapers in a closed-lid garbage can.
- Washing their hands thoroughly and frequently when ill with diarrhea, or when caring for someone with diarrhea. Hands should be scrubbed for at least 15–20 seconds after cleaning the bathroom; after using the toilet or helping someone use the toilet; after changing diapers; before handling food; and before eating.

Discuss transmission risks that may result from oral-anal sexual contact. Latex barrier protection (e.g., dental dam) may prevent the spread of hepatitis A to a case's sexual partners as well as being a way to prevent exposure to and transmission of other fecal-oral pathogens.

### **International Travel**

Travelers should pay attention to what they eat and drink. Recommendations to travelers include:

- "Boil it, cook it, peel it, or forget it."
- Drink only bottled or boiled water, keeping in mind that bottled carbonated beverages are safer than bottled noncarbonated ones.
- Ask for drinks without ice, unless the ice is made from bottled or boiled water.
- Avoid popsicles and flavored ices that may have been made with contaminated water.
- Eat foods that have been thoroughly cooked and are still hot and steaming.
- Avoid raw vegetables and fruits that cannot be peeled. Vegetables like lettuce are easily contaminated and are very hard to wash well.
- Peel their own raw fruits or vegetables, and do not eat the peelings.
- Avoid foods and beverages from street vendors.



## **Chemoprophylaxis:**

When indicated, hepatitis A vaccine or immune globulin (IG) can be administered to contacts of a case of hepatitis A to prevent infection. Hepatitis A vaccine and IG have not been proven to be effective for contacts of a case of hepatitis E. The decision to use vaccine or IG should take into account patient characteristics, including age and medical conditions. Standard IG is a concentrated solution of antibodies prepared from pooled human plasma. IG should be administered as soon as possible after exposure, and it is 80–90% effective in preventing hepatitis A if given within 14 days of exposure. The vaccine is composed of inactivated whole-viruses and is just as effective as IG in preventing disease if given within 14 days of exposure.

Vaccination is recommended for:

- Healthy persons aged 12 months to 40 years

IG is recommended for:

- Persons >40 years
- Infants <12 months
- Immunocompromised persons
- Persons who have had chronic liver disease
- Persons for whom vaccination is contraindicated

To be offered vaccine or IG, the following conditions should be met:

- The case is confirmed or suspect. Laboratory confirmation of HAV is generally obtained before administering prophylaxis.
- Exposure occurred within the patient's infectious period. A person with contact to the case outside the infectious period is not considered a case contact.
- Less than 14 days have passed since the last exposure occurred.

Persons who have received one dose of hepatitis A vaccine at least 1 month before a hepatitis A exposure do not need prophylaxis. The safety of hepatitis A vaccine for pregnant women has not been determined. But there is no evidence that it is harmful to either pregnant women or their unborn babies. Pregnancy or lactation is not a contraindication to IG use. Persons administered IG for whom hepatitis A vaccine also is recommended for other reasons should receive a dose of vaccine simultaneously with IG.

The Bureau of Epidemiology (BOE) at the Utah Department of Health supplies IG to local health departments to administer to contacts of confirmed or highly suspect Utah hepatitis A cases. This IG can be stored at the local health department by arrangement with BOE. BOE does not supply IG dispensed for any other reason (e.g. preexposure prophylaxis, contact to a non-Utah case, etc.). In such circumstances, IG recipients or local health departments are responsible for the cost.

IG is administered in a single dose at the following dosage: 0.02 mL/kg. Plan to use approximately 0.5 mL IG per 50 lbs. Use the following algorithm to determine the amount of IG to administer:

$$\frac{\quad}{\text{Person's weight in lbs}} \times 0.454 \times 0.02 = \boxed{\quad} \text{ mL IG}$$

Vaccination for hepatitis A is recommended for travelers to areas where hepatitis A is endemic. However, travelers should receive IG before travel under the following circumstances:

- If they are allergic to a component of the vaccine or elect not to receive vaccine
- If they are <2 years old (vaccine is not licensed for this age group)
- If they are traveling to an endemic area in <4 weeks, they may receive vaccine and IG at the same time (in different anatomical sites)

### **Vaccine:**

Two inactivated whole-virus vaccines for hepatitis A are currently licensed in the United States for use in persons 12 months of age and older. This vaccine is approved for individuals over the age of 2 and is thought to provide protection for at least 10 years. Both vaccines are highly immunogenic and highly effective in preventing clinical hepatitis A. In 2005 the Advisory Committee on Immunization Practices (ACIP) recommended that hepatitis A vaccination be included into the routine childhood vaccination schedule and should be administered to infants 12-23 months of age. Additionally, ACIP has recommended that vaccination programs target children 2-18 years of age living in states, counties, or communities with an increased risk of hepatitis A infection. The safety of hepatitis A vaccine for pregnant women has not been determined. But there is no evidence that it is harmful to either pregnant women or their unborn babies.

Vaccination should also be considered for persons at high risk of contracting hepatitis A. Persons who should be vaccinated include the following:

- Persons traveling to or working in countries with high or intermediate rates of hepatitis A, such as Central or South America, the Caribbean, Mexico, Asia (except Japan), Africa, and southern or eastern Europe. The vaccine series should be started at least one month before traveling.
- Men who have sex with men.
- Injecting and non-injecting drug users.
- Persons with chronic liver disease (not just infection), including those who are awaiting or have received liver transplants.
- Persons who receive clotting factor concentrates.
- Persons who have occupational risk for infection; specifically, those who work with HAV-infected primates or with HAV in a research laboratory setting. Sewage workers do not need to be vaccinated.

The hepatitis A vaccine should be administered in 2 doses, 6-12 months apart. Both vaccines have pediatric and adult formulations. The hepatitis A vaccine is not protective until two weeks after receiving the initial dose.

## Isolation and quarantine requirements:

**Isolation:** Persons diagnosed with hepatitis A that are associated with school or daycare should be excluded for 8 days after the onset of jaundice. Food handlers should also be excluded until 8 days after the onset of jaundice.

**NOTE:** A food handler is any person directly preparing or handling food. This can include a patient care or childcare provider.

**Hospital:** Enteric precautions for 8 days after onset of jaundice.

**Quarantine:** No restrictions except for food handling facility employees, who shall be excluded from their occupations for 28 days, unless they receive a prophylactic dose of hepatitis A vaccine or immune globulin (IG) within 14 days of exposure. (Exceptions to this exclusion are documentation of HAV vaccination or demonstrated serologic evidence of immunity to HAV.)

## ✓ CASE INVESTIGATION

### Reporting:

All cases of hepatitis A should be reported to public health immediately.

### Case definition:

#### Hepatitis A, acute (2000):

##### Clinical Case Definition

An acute illness with:

- Discrete onset of symptoms, and
- Jaundice or elevated serum aminotransferase levels.

##### Laboratory Criteria

- Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive.

##### Case Classification

*Confirmed:* a case that meets the clinical case definition and is laboratory confirmed or a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms)

### Case Investigation Process:

- Local and state health departments should be immediately notified.
- Food handlers should be excluded from work until 8 days after the onset of jaundice.
- Daycare center contacts should be excluded until 8 days after the onset of jaundice.
- All case contacts should be identified and appropriately managed (explained in detail below).

### Outbreaks:

CDC defines a food-borne outbreak as, “an incident in which two or more persons experience a similar illness resulting from the ingestion of a common food”. In order to

confirm an outbreak of hepatitis A, detection of immunoglobulin M anti-hepatitis A virus in serum from two or more persons who consumed epidemiologically implicated food is necessary. The source of the infection should be identified and measures to identify additional ill persons and/or to remove the source from consumers should be taken.

### **Identification of case contacts and management:**

A case contact meets one or more of the following descriptions:

1. **Close personal contacts** include household members, sexual contacts, drug-using contacts, and persons who shared utensils or cups with the case.
2. **Daycare center contacts.**
3. **Close contacts in a hospital or long-term-care setting**, especially of incontinent cases.
4. **Other food handlers** if the case is a food handler diagnosed with hepatitis A.

### **Daycare**

If a confirmed case of hepatitis A occurs in a childcare setting, parents and staff must be notified. Hepatitis A fact sheets should also be sent with the letter. Control of hepatitis A in childcare settings includes the following steps:

- When the case is an employee or child enrolled in a center in which all children are toilet-trained, vaccine or IG is recommended for susceptible employees in contact with the case and for all susceptible children in the same room as the case.
- When a HAV infection is identified in an employee or a child or in the household contacts of two of the enrolled children in a daycare center where children are not toilet-trained, vaccine or IG is recommended for all susceptible employees and all susceptible, enrolled children in the facility. During the six weeks after the last case is identified, susceptible new employees and children should also receive vaccine or IG.
- Strictly enforce policies about handwashing (with children and staff) and about disinfecting objects and environmental surfaces with appropriate disinfectants, such as bleach solutions.
- Make sure all parents and staff understand that they must notify the program if any person in their household is diagnosed with hepatitis A.
- If recognition of an outbreak in a childcare setting is delayed by three or more weeks from the onset of the index case or if illness has occurred in three or more families, vaccine or IG should be considered for household members of all center attendees.

Note that childcare setting employees who prepare food, feed children, or administer medications to attendees are considered food handlers and must follow the isolation and quarantine requirements for food handling facility employees who are contacts of cases of hepatitis A.

### **School**

Hepatitis A occurring in a school setting usually does not pose a significant risk of transmission, and prophylaxis is usually not indicated. However, vaccine or IG may be given to those who have personal contact with a case during the case's infectious period (e.g., sharing food or eating or drinking utensils with a case). If a case of hepatitis A occurs in a kindergarten or preschool class or in a class where hygiene may not be optimal, more stringent control measures may be needed. Strictly enforce handwashing

and cleanliness policies and ensure that all bathrooms are properly supplied with soap, paper towels, and toilet paper. Request that all parents and staff notify the school if any person in their household is diagnosed with hepatitis A.

### **Community Residential Programs**

Actions taken in response to a case of HAV infection in a community residential program should be handled on a case-by-case basis. Management of contacts will depend on the level of hygiene of the case and the type of facility. Roommates and anyone sharing food or eating or drinking utensils should be considered household contacts and should be given vaccine or IG within 14 days of exposure. If hepatitis A occurs in a staff member of a residential program, the case should be considered a food handler if there was an opportunity to feed, distribute medication, prepare foods, or perform dental procedures during the two weeks prior to symptom onset.

### **Infected Food Handler**

A confirmed case of hepatitis A in a food handler is a potentially serious event and requires that risk for both coworkers and the public be assessed as quickly as possible. If a food handler is a laboratory-confirmed case of hepatitis A, all other food handling employees in the facility must receive vaccine or IG within two weeks of exposure. Unless the food handling facility employee contacts can produce documentation of vaccination against hepatitis A, can show immunity to HAV by serology, or unless they receive vaccine or IG within 2 weeks of exposure, they must be excluded from work. The same exclusion criteria apply to any food handling contacts of any confirmed case. In order to determine if the public needs to be notified of possible exposure to HAV, a complete food handling history of the case for the two weeks before symptom onset needs to be reviewed. This review should include dates worked, job duties, foods prepared, and whether gloves or other barrier protection were used by the food handler.

Vaccine or IG administration to patrons is usually not recommended but should be considered if:

- During the time when the food handler was likely to be infectious, the food handler both directly handled cooked foods or foods that were served uncooked and had diarrhea or poor hygienic practices; and
- Patrons can be identified and treated within two weeks after the exposure. In settings where repeated exposures to HAV might have occurred (e.g., institutional cafeterias), stronger consideration of more widespread IG use might be warranted.

If it is determined that patrons would benefit from vaccine or IG administration, the local health department will be responsible for posting public notices, issuing press releases, and/or holding press conferences to identify and inform patrons at risk and in coordinating the administration of vaccine or IG to individuals.

### **Hospitals**

Administration of vaccine or IG to hospital personnel caring for infected patients is not routinely indicated, unless an outbreak is occurring. However, if a hospital staff member is diagnosed with hepatitis A and can be considered a food handler, then the food handler guidelines must be followed.

## REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.1

Control of Communicable Diseases Manual (18<sup>th</sup> Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26<sup>th</sup> Edition), Larry K. Pickering MD, Ed; 2003.

Principles and Practice of Infectious Disease (6<sup>th</sup> Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.